## What is Claimed:

- 1. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:
  - a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA expressed within the cell;
  - b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
  - c) a spacer region that separates the 3' splice region from the target binding domain; and
  - a nucleotide sequence to be trans-spliced to the target premRNA;

- 2. A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:
  - a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA expressed within the cell;

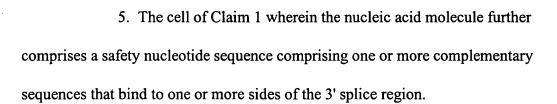
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target premRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

- 3 A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:
  - a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA expressed within the cell;
  - b) a 5' splice site;
  - a spacer region that separates the 5' splice site from the target binding domain; and
  - a nucleotide sequence to be trans-spliced to the target premRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

4. The cell of claim 1 wherein the nucleic acid molecule further comprises a 5' donor site.



- 6. The cell of Claim 1 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.
- 7. The cell of Claim 1 wherein the nucleotide sequences to be transspliced to the target pre mRNA encode a factor VIII polypeptide.
- 8. The cell of claim 1 wherein the nucleotide sequences to be trans-spliced to the target pre-mRNA encodes exons 23-26 of canine or human factor VIII protein or exons 16-26 of murine human factor VIII protein.
- 9. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:
  - a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA expressed within the cell;
  - b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
  - c) a spacer region that separates the 3' splice region from the target binding domain; and

d) a nucleotide sequence to be trans-spliced to the target premRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

- 10. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:
  - a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA expressed within the cell;
  - b) a 3' splice acceptor site;
  - c) a spacer region that separates the 3' splice region from the target binding domain; and
  - d) a nucleotide sequence to be trans-spliced to the target premRNA;

- 11. A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:
  - a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA

expressed within the cell;

- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- a nucleotide sequence to be trans-spliced to the target premRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

- 12. The cell of claim 9 wherein the nucleic acid molecule further comprises a 5' donor site.
- 13. A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;

- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target premRNA;

under conditions in which a portion of the nucleic acid molecule is transspliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

14. A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target premRNA; under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target premRNA to form a chimeric RNA within the cell.

15. A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of
  the nucleic acid molecule to a factor VIII pre-mRNA
  expressed within the cell;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target premRNA;

- 16. A method of claim 13 wherein the nucleic acid molecule further comprises a 5' donor site.
- 17. The method of claim 13, wherein the chimeric RNA molecule comprises sequences encoding a translatable protein.

## 18. A nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and
- e) a nucleotide sequence to be trans-spliced to the target premRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

## 19. A nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site;

- c) a spacer region that separates the 3' splice region from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and
- e) a nucleotide sequence to be trans-spliced to the target premRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

## 20. A nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII pre-mRNA expressed within the cell;
- b) a 5' splice site;
- a spacer region that separates the 5' splice site from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 5' splice site; and
- e) a nucleotide sequence to be trans-spliced to the target premRNA;



- 21. The nucleic acid molecule of claim 18 wherein the nucleic acid molecule further comprises a 5' donor site.
- 22. The nucleic acid molecule of claim 18 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.
- 23. The nucleic acid molecule of claim 18 wherein the nucleotide to be trans-spliced to the target pre-mRNA encodes a translatable factor VIII polypeptide and/or a marker protein.
- 24. The nucleic acid molecule of claim 18 wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes exons 23-26 of canine or human factor VIII protein or exons 16-26 of murine human factor VIII protein.25. The nucleic acid molecule of claim 20 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.
  - 26. The nucleic acid molecule of claim 20 wherein the nucleotide

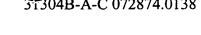
sequence to be trans-spliced to the target pre-mRNA encodes a factor VIII polypeptide and/or a marker gene sequence.

- 27. The nucleic acid molecule of claim 20 wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes exons 23-26 of the factor VIII protein.
- 28. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:
  - a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII protein premRNA expressed within the cell;
  - b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
  - a spacer region that separates the 3' splice region from the target binding domain; and
  - d) a nucleotide sequence to be trans-spliced to the target premRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.
  - 29. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to factor VIII protein pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target premRNA;

- 30. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:
  - a) one or more target binding domains that target binding of the nucleic acid molecule to a factor VIII protein premRNA expressed within the cell;
  - b) a 5' splice site;
  - c) a spacer region that separates the 5' splice site from the target binding domain; and
  - d) a nucleotide sequence to be trans-spliced to the target premRNA;





- 31. The vector of claim 28 wherein the nucleic acid molecule further comprises a 5' donor site.
  - 32. The vector of claim 28 wherein said vector is a viral vector.
- 33. The vector of claim 32 wherein in said viral vector is an adeno-associated viral vector.
- 34. A composition comprising a physiologically acceptable carrier and a nucleic acid molecule according to any of claims 28-33.